REMARKS

I. Pending Claims

Claims 21-40 are pending in the application. Claims 30, 32-34 and 37-40 are withdrawn as being drawn to non-elected inventions. Claim 21 has been amended. Claims 21-29, 31, 35, and 36 are under active consideration.

To expedite prosecution, part c) of claim 21 has been deleted. Entry of this amendment is respectfully requested.

Applicants reserve the right to prosecute non-elected subject matter in subsequent divisional applications.

II. Comments Regarding Restriction Requirement

Applicants affirm the election with traverse of Group 23, which corresponds to claims 23-29, and 31 (replacing original claims 3-4, and 9-14) drawn to polynucleotides. Applicants thank the Examiner for rejoining claims 21, 22, 35, and 36, drawn to polypeptides, with the claims of Group 23 (Office Action, December 3, 2003; p. 2).

III. Rejoinder

Applicants reiterate their request that claims 32-34, 39, and 40, drawn to methods of using the polynucleotides, be rejoined, and in addition, request that claims 37 and 38, drawn to methods of using the polypeptides, be rejoined per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of product claims, for rejoinder of process claims covering the same scope of products. Applicants request that claims 32-34, 39, and 40 be rejoined and examined upon allowance of any of the claims drawn to the polynucleotides of Group 23 and that claims 37 and 38 be rejoined and examined upon allowance of any of the claims drawn to the polypeptides.

IV. Objection to the Specification

An abstract was added to the specification to comply with 37 CFR 1.72(b). In addition, Applicants have replaced the heading entitled "BRIEF DESCRIPTION OF THE FIGURES AND TABLES" with the heading, "Brief Description of the Drawings" as described in MPEP 608.01(f) and 37 CFR 1.74, *Reference to drawings*. Replacement of this heading serves to correctly describe Applicants' figures and tables.

V. Indefiniteness rejections under 35 U.S.C. § 112, second paragraph

Claims 22-29, 31 and 35-36 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite in the recitation of the phrases "naturally-occurring," "biologically active fragment," and "RNA equivalent." The rejection is traversed.

The Office Action asserts that the phrase "biologically active" is indefinite. While not conceding as to the propriety of this rejection, that phrase has been deleted from the claims in order to expedite prosecution of the subject application.

In addition, the Office Action alleged that the phrase "naturally occurring" is indefinite. Such, however, is not the case. In pertinent part, claim 21 recites "a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:7," and claim 31 recites "a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:25." Hence, "naturally occurring" merely refers to the source of the amino acid or polynucleotide sequence, *i.e.*, the sequence must be found in nature. However, the polypeptide or polynucleotide recited by the claim can be made by any means, such as isolation from nature or manufacture by chemical or recombinant methods. It is the amino acid or polynucleotide *sequence* which must be found in nature.

With regard to the rejection concerning the phrase, "RNA equivalent," Applicants submit that an "RNA equivalent" in reference to a DNA molecule, is composed of the same linear sequence of nucleotides as the reference DNA molecule with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

A. The Claims Must be Examined on the Basis of Whether One Having Ordinary Skill in the Art Would be Able to Determine the Scope of the Claim

One of skill in the art would readily be able to determine the meaning of the term "an RNA equivalent." The M.P.E.P. provides guidelines to Examiners for rejections under 35 U.S.C. § 112, second paragraph as follows:

> ...a full explanation of the deficiency of the claims should be supplied. Whenever possible, identify the particular term(s) or limitation(s) which render the claim(s) indefinite and state why such term or limitation renders the claim indefinite. If the scope of the claimed subject matter can be determined by one having ordinary skill in the art, a rejection using this form paragraph would not be appropriate (M.P.E.P. § 706.03(d)).

Therefore, claims must be examined on the basis of whether one having ordinary skill in the art would be able to determine the scope of the claim and, if a rejection is made, reasons must be provided why the claim is indefinite. Applicants submit that the Examiner has not provided any reasons or evidence why the cited phrase is indefinite and/or why one having ordinary skill in the art could not determine the scope of the claim. For this reason alone, the rejection is improper and should be withdrawn.

B. The Term "an RNA equivalent" is Well-Understood in the Art

Applicants submit that "an RNA equivalent" has the plain meaning of the words, and that the skilled artisan would understand that "an RNA equivalent" in reference to a DNA molecule, is composed of the same linear sequence of nucleotides as the reference DNA molecule with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose.

As a general rule, claim language carries the ordinary and accustomed meaning of the words in their normal usage in the field of invention (Toro Co. v. White Consol. Indus., 199 F.3d 1295, 53 USPQ2d 1065, 1067 Fed. Cir. 1999). The dictionary defines "RNA" as "any of various nucleic acids that contain ribose and uracil as structural components and are associated with the control of cellular

chemical activities", and "equivalent" as "corresponding or virtually identical especially in effect or function" and "having the same chemical combining capacity, i.e., *equivalent* quantities of two elements" (Reference No. 3; Merriam-Webster's Collegiate Dictionary; Merriam-Webster OnLine: http://www.m-w.com).

Applicants also call the Examiner's attention to M.P.E.P § 2111.01, which states that "[p]lain meaning refers to the meaning given to the term by those of ordinary skill in the art." Thus, one of skill in the art would understand the meaning of the term "an RNA equivalent" within the context of the claims.

C. The Specification Contains Adequate Support for the Meaning of the Term, "an RNA equivalent"

There is adequate definition of the term "an RNA equivalent" in the Specification. An inventor may act as his own lexicographer and use the Specification to supply new meanings for terms implicitly or explicitly (Markman v. Westview Instruments, Inc., 52 F.3d 967, 979-80, 34 USPQ2d 1321, 1330 (Fed. Cir. 1995) en banc, aff'd 517 U.S. 370 (1996)). On p. 45, lines 1-4, the Specification describes how polynucleotides encoding MECHP may be used for diagnostic purposes: "The polynucleotides which may be used include oligonucleotide sequences, complementary RNA and DNA molecules, and PNAs." Again, Applicants submit that in the context of this description, the skilled artisan would understand that "an RNA equivalent" in reference to a DNA molecule, is composed of the same linear sequence of nucleotides as the reference DNA molecule with the exception that all occurrences of the nitrogenous base thymine are replaced with uracil, and the sugar backbone is composed of ribose instead of deoxyribose. For at least the above reasons, the meaning of the claims is clear.

Based at least upon these arguments, Applicants request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

VI. Utility rejection under 35 U.S.C. § 101 and § 112, first paragraph

Claims 22-29, 31 and 35-36 stand rejected under 35 U.S.C. § 101 and § 112, first paragraph, based on the allegation that the claimed invention lacks patentable utility. The rejection alleges in

particular that:

- "...the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility". (Office Action, December 3, 2003; page 5).
- "...since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention". (Office Action, December 3, 2003; page 17).

The rejection of Claims 22-29, 31 and 35-36 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well known to one of ordinary skill in the art.

The invention at issue is a polypeptide and its corresponding polynucleotide encoding a gap junction protein, beta 4, connexin, which is expressed in nervous, reproductive and gastrointestinal tissue in humans. The claimed invention has numerous practical, beneficial uses in toxicology testing, drug development, and the diagnosis of disease, none of which requires knowledge of how the polypeptide coded for by the polynucleotide actually functions.

Applicants submit with this paper two expert Declarations under 37 C.F.R. § 1.132, with respective attachments, and ten (10) scientific references filed before or shortly after the November 23, 1998 priority date of the instant application. The Rockett Declaration and the Iyer Declaration, and the ten (10) references establish that, prior to the filing dates of the provisional applications to which the subject application is benefitted priority, it was well-established in the art that:

> polynucleotides derived from nucleic acids expressed in one or more tissues and/or cell types can be used as hybridization probes -- that is, as tools -- to survey for and to measure the presence, the absence, and the amount of expression of their cognate gene;
>
> with sufficient length, at sufficient hybridization stringency, and with sufficient wash stringency -- conditions that can be routinely established -- expressed polynucleotides, used as probes, generate a signal that is specific to the cognate gene, that is, produce a gene-specific expression signal;

expression analysis is useful, *inter alia*, in drug discovery and lead optimization efforts, in toxicology, particularly toxicology studies conducted early in drug development efforts, and in phenotypic characterization and categorization of cell types, including neoplastic cell types;

each additional gene-specific probe used as a tool in expression analysis provides an additional gene-specific signal that could not otherwise have been detected, giving a more comprehensive, robust, higher resolution, statistically more significant, and thus more useful expression pattern in such analyses than would otherwise have been possible;

biologists, such as toxicologists, recognize the increased utility of more comprehensive, robust, higher resolution, statistically more significant results, and thus want each newly identified expressed gene to be included in such an analysis;

nucleic acid microarrays increase the parallelism of expression measurements, providing expression data analogous to that provided by older, lower throughput techniques, but at substantially increased throughput;

accordingly, when expression profiling is performed using microarrays, each additional gene-specific probe that is included as a signaling component on this analytical device increases the detection range, and thus versatility, of this research tool;

biologists, such as toxicologists, recognize the increased utility of such improved tools, and thus want a gene-specific probe to each newly identified expressed gene to be included in such an analytical device;

the industrial suppliers of microarrays recognize the increased utility of such improved tools to their customers, and thus strive to improve salability of their microarrays by adding each newly identified expressed gene to the microarrays they sell;

it is not necessary that the biological function of a gene be known for measurement of its expression to be useful in drug discovery and lead optimization analyses, toxicology, or molecular phenotyping experiments;

failure of a probe to detect changes in expression of its cognate gene does not diminish the usefulness of the probe as a research tool; and

failure of a probe completely to detect its cognate transcript in any single expression analysis experiment does not deprive the probe of usefulness to the community of users who would use it as a research tool.

The Patent Examiner does not dispute that the claimed polynucleotide can be used as a probe in cDNA microarrays and used in gene expression monitoring applications. Instead, the Patent Examiner contends that the claimed polynucleotide cannot be useful without precise knowledge of its biological function, or the biological function of the polypeptide it encodes. But the law has never required knowledge of biological function to prove utility. It is the claimed invention's uses, not its functions, that are the subject of a proper analysis under the utility requirement.

In any event, as demonstrated by the Rockett Declaration and the Iyer Declaration the person of ordinary skill in the art can achieve beneficial results from the claimed polynucleotide in the absence of any knowledge as to the precise function of the protein encoded by it. The uses of the claimed polynucleotide in gene expression monitoring applications are in fact independent of its precise biological function.

VII. Enablement rejection under 35 U.S.C. § 112, first paragraph

Claims 20-29, 31, 35-36 are rejected for allegedly failing to meet the requirements of 35 U.S.C. § 112, first paragraph, on the grounds that the Specification does not provide an enabling disclosure commensurate in scope with the claims. In particular, the Examiner alleges that "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention" (*see* Office Action, p. 17). Applicants traverse the rejection for at least the following reasons.

As set forth in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971):

> The first paragraph of § 112 requires nothing more than **objective enablement**. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.
>
> As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first

> paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Applicants submit that the disclosure amply enables the claimed invention. Given the sequence of SEQ ID NO:25, one of ordinary skill in the art could readily identify a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence of SEQ ID NO:25, using well known methods of sequence analysis without any undue experimentation. For example, the identification of relevant polynucleotides could be performed by hybridization and/or PCR techniques that were well-known to those skilled in the art at the time the subject application was filed and/or described throughout the Specification of the instant application. See, e.g., p. 45, lines 7-11, and Example IX at p. 58. Thus, one skilled in the art need not make and test vast numbers of polynucleotides. Instead, one skilled in the art need only screen a cDNA library or use appropriate PCR conditions to identify relevant polynucleotides that already exist in nature. The skilled artisan would also know how to use the claimed polynucleotides, for example in expression profiling, disease diagnosis, or detection of related sequences as discussed above. The specification also describes the expression vectors into which the claimed variants and fragments could be inserted, and the construction of fusion proteins (*see also* pp. 32-33).

Applicants respectfully point out that the claims of the instant application are drawn to **naturally occurring** variants. Thus it is not necessary to screen every conceivable variant which might be made using recombinant methods, as all that is claimed are those variant sequences which are found in nature. Through the process of natural selection, nature will have determined the appropriate sequences.

Further, the Examiner requires working examples (Office Action, p. 18). There is no such requirement under the law to provide "working examples." As set forth in *In re Borkowski,* 164 USPQ 642, 645 (CCPA 1970) (footnote omitted):

> However, as we have stated in a number of opinions, a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

See also M.P.E.P. 2164.02 as follows:

> Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic"... A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved.

Thus, there is no requirement under the law to provide "working examples" of what is claimed. Rather, one looks to whether the specification provides a description of how to make what is claimed. The present specification provides the requisite description.

Contrary to the standard set forth in *Marzocchi* and *Borkowski*, the Examiner has failed to provide any ***reasons*** why one would doubt that the guidance provided by the present specification would enable one to make and use the recited polynucleotides and polypeptides. Hence, a *prima facie* case for non-enablement has not been established. For at least the above reasons, withdrawal of the enablement rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

The claims have also been rejected for lack of utility under 35 U.S.C. §112, first paragraph. To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons.

VIII. Written description rejection under 35 U.S.C. § 112, first paragraph

Claims 21, 23, 26-29, 31 and 35 have been rejected under the first paragraph of 35 U.S.C. § 112 for an alleged lack of an adequate written description. Applicants note that the polypeptide biologically-active fragments of claim 21 have been canceled; therefore, the rejection on this basis is moot.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that :

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met (footnotes omitted).

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

SEQ ID NO:7 and SEQ ID NO:25 are specifically disclosed in the application (*see*, for example, the Sequence Listing and p. 2, lines 3-22). Variants of SEQ ID NO:7 and SEQ ID NO:25 are described, for example, at p. 23, line 26 to p. 27, line 7. Incyte clones in which nucleic acids encoding each MECHP were identified are described in columns 3 and 4 of Table 1. Chemical and structural features of SEQ ID NO:7 are described, for example, on page 12, lines 13-29. Expression data for SEQ ID NO:25 are described in Table 4. Given SEQ ID NO:7, one of ordinary skill in the art would recognize a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:25. Accordingly, the Specification provides an adequate written description of the recited polypeptide and polynucleotide sequences.

1. The present claims specifically define the claimed genus through the recitation of chemical structure

Court cases in which "DNA claims" have been at issue (which are hence relevant to claims to proteins encoded by the DNA) commonly emphasize that the recitation of structural features or chemical or physical properties are important factors to consider in a written description analysis of

such claims. For example, in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), the court stated that:

> If a conception of a DNA requires a precise definition, such as by structure, formula, chemical name or physical properties, as we have held, then a description also requires that degree of specificity.

In a number of instances in which claims to DNA have been found invalid, the courts have noted that the claims attempted to define the claimed DNA in terms of functional characteristics without any reference to structural features. As set forth by the court in *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997):

> In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.

Thus, the mere recitation of functional characteristics of a DNA, without the definition of structural features, has been a common basis by which courts have found invalid claims to DNA. For example, in *Lilly*, 43 USPQ2d at 1407, the court found invalid for violation of the written description requirement the following claim of U.S. Patent No. 4,652,525:

> 1. A recombinant plasmid replicable in procaryotic host containing within its nucleotide sequence a subsequence having the structure of the reverse transcript of an mRNA of a vertebrate, which mRNA encodes insulin.

In *Fiers*, 25 USPQ2d at 1603, the parties were in an interference involving the following count:

> A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.

Party Revel in the *Fiers* case argued that its foreign priority application contained an adequate written description of the DNA of the count because that application mentioned a potential method for isolating the DNA. The Revel priority application, however, did not have a description of any particular DNA structure corresponding to the DNA of the count. The court therefore found that the Revel priority application lacked an adequate written description of the subject matter of the count.

Thus, in *Lilly* and *Fiers*, nucleic acids were defined on the basis of functional characteristics and were found not to comply with the written description requirement of 35 U.S.C. §112; *i.e.*, "an mRNA of a vertebrate, which mRNA encodes insulin" in *Lilly*, and "DNA which codes for a human fibroblast interferon-beta polypeptide" in *Fiers*. In contrast to the situation in *Lilly* and *Fiers*, the claims at issue in the present application define polynucleotides and polypeptides in terms of chemical structure, rather than functional characteristics. For example, the "variant language" of independent claim 21 and independent claim 31 recites chemical structure to define the claimed genus:

21. "An isolated polypeptide selected from the group consisting of:

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:7."

31. "An isolated polynucleotide selected from the group consisting of::

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:25."

From the above it should be apparent that the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:7 and SEQ ID NO:25. In the present case, there is no reliance merely on a description of functional characteristics of the polynucleotides or polypeptides recited by the claims. The polynucleotides and polypeptides defined in the claims of the present application recite structural features, and cases such as *Lilly* and *Fiers* stress that the recitation of structure is an important factor to consider in a written description analysis of claims of this type. By failing to base its written description inquiry "on whatever is now claimed," the Office Action failed to provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Lilly* and *Fiers*.

2. The present claims do not define a genus which is "highly variant"

Furthermore, the claims at issue do not describe a genus which could be characterized as "highly variant." Available evidence illustrates that the claimed genus is of narrow scope.

In support of this assertion, the Examiner's attention is directed to the enclosed reference by Brenner et al. ("Assessing sequence comparison methods with reliable structurally identified distant evolutionary relationships," Proc. Natl. Acad. Sci. USA (1998) 95:6073-6078). Through exhaustive analysis of a data set of proteins with known structural and functional relationships and with <90% overall sequence identity, Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that ≥40% identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

The "variant language" of the present claims recites, for example, polynucleotides encoding "a naturally occurring polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:25." This variation is far less than that of all potential polynucleotides encoding MECHP proteins.

3. The state of the art at the time of the present invention is further advanced than at the time of the *Lilly* and *Fiers* applications

In the *Lilly* case, claims of U.S. Patent No. 4,652,525 were found invalid for failing to comply with the written description requirement of 35 U.S.C. §112. The '525 patent claimed the benefit of priority of two applications, Application Serial No. 801,343 filed May 27, 1977, and Application Serial No. 805,023 filed June 9, 1977. In the *Fiers* case, party Revel claimed the benefit of priority of an Israeli application filed on November 21, 1979. Thus, the written description inquiry in those case was based on the state of the art at essentially at the "dark ages" of recombinant DNA technology.

The present application has a priority date of September 2, 1998. Much has happened in the development of recombinant DNA technology in the 21 or more years from the time of filing of the applications involved in *Lilly* and *Fiers* and the present application. For example, the technique of polymerase chain reaction (PCR) was invented. Highly efficient cloning and DNA sequencing technology has been developed. Large databases of protein and nucleotide sequences have been compiled. Much of the raw material of the human and other genomes has been sequenced. With these

remarkable advances one of skill in the art would recognize that, given the sequence information of SEQ ID NO:7 and SEQ ID NO:25, and the additional extensive detail provided by the subject application, the present inventors were in possession of the claimed polynucleotide variants at the time of filing of this application.

4. Summary

The Office Action failed to base its written description inquiry "on whatever is now claimed." Consequently, the Action did not provide an appropriate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in cases such as *Lilly* and *Fiers*. In particular, the claims of the subject application are fundamentally different from those found invalid in *Lilly* and *Fiers*. The subject matter of the present claims is defined in terms of the chemical structure of SEQ ID NO:7 or SEQ ID NO:25. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polynucleotides and polypeptides defined by the present claims is adequately described, as evidenced by Brenner et al. Furthermore, there have been remarkable advances in the state of the art since the *Lilly* and *Fiers* cases, and these advances were given no consideration whatsoever in the position set forth by the Office Action. For at least the reasons mentioned, withdrawal of the written description rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

CONCLUSION

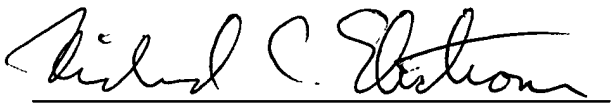
In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108.**

Respectfully submitted,
INCYTE CORPORATION

Date: 01 March 2004



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Attachment(s):

1. Declaration of John C. Rockett, Ph.D., under 37 C.F.R.§1.132, with Exhibits A - Q
2. Declaration of Vishwanath R. Iyer, Ph.D., under 37 C.F.R. § 1.132 with Exhibits A - E
3. Merriam-Webster's Collegiate Dictionary; Merriam-Webster OnLine: http://www.m-w.com).